SYLLABUS

M.S. (Pharm.)

Medicinal Chemistry

M.S. (Pharm.) Medicinal Chemistry

Course No.	Course Name	Credits
Semester-I		
MC-510	Basics of Drug Action	2
** MC-511	Spectral Analysis	2
MC-520	Logic in Organic Synthesis-I	3
*** MC-530	Separation Techniques	1
**** PE-510	Pharmaceutical Preformulation - I	1
**** MC-540	Industrial Process and Scale-up Techniques	1
* GE-510	Biostatistics	2
GE-511	Seminar	1
LG-510	General Lab Experience	3
	Total Credits	**16**
Semester-II		
MC-610	Drug Design	2
MC-620	Logic In Organic Synthesis-II	3
MC-630	Structure and Function of Biomolecules	2
MC-650	Stereochemistry and Drug Action	2
**** PE-660	Solid State Pharmaceutics	1
@ PC-610	Drug Metabolism	1
GE-611	Seminar	1
LS-610	General Lab Experience in the Area of Specialization	2
	Total Credits	**14**
Semester-III		
Project (22 weeks)		
TH-598	Synopsis	5
TH-599	Presentation	3
	Total Credits	**8**
Semester-IV		
TH-698	Thesis	9
TH-699	Defence of Thesis	3
	Total Credits	**12**
	Grand Credits (I to IV Semesters)	**50**

Note:
- * Common in all disciplines
- ** Common in MC, PA, PE, BT
- *** Common in MC, PA, PE, PC, BT
- **** Common in MC, PA, PE
- @ Common in MC, PE, PC, RT

M.S. (Pharm.) Medicinal Chemistry
SEMESTER - I

MC 510 - Basics of Drug Action (2 Credits)	
1.	**Structure:** 2D vs 3D. Chemical structure *vs.* electronic structure. Electronic structure of ketenes and its importance in reactivity. Electronic effect on Diels-Alder reaction, Symmetry using group theory and symmetry elements. Graph theory and 2D structure.
2.	**Energy:** Free energy, Energy concept and its importance in drug action. First, Second and Third laws of thermodynamics and the principles derived from these laws which are of significance to drug action.
3.	**Thermodynamics:** Free energy and Relationship between thermodynamics and statistics. Importance of chemical potential in drug action. Thermodynamic cycle. Statistical thermodynamics in predicting the structure of biomolecules and their interaction with drug molecules. Macromolecular vs. micromolecular correlation using thermodynamics and statistical thermodynamics.
4.	**Interactions:** *Inter*- and *intra*-molecular interactions. Weak interactions in drug molecules. Chirality and drug action. Covalent, ion-ion, ion-dipole, Hydrogen bonding, C-H hydrogen bonding, dihydrogen bonding, Charge transfer complex, Hydrophobic interaction, Van der Waals interactions, London dispersion forces, and associated energies.
5.	**Drug-receptor interactions, Receptor theories and drug action:** Occupancy Theory, Rate Theory, Induced Fit Theory, Macromolecular perturbation theory, Activation-Aggregation theory.
6.	**Topological and stereochemical consideration**: Spatial arrangement of atoms, Drug and receptor chirality, Geometric isomers, Conformational isomers, Ring topology,
7.	**Enzyme Kinetics:** Enzyme kinetics in drug action. Do all molecules of an enzyme have the same kinetics? Mechanisms of enzyme catalysis, Electrostatic catalysis and desolvation. Covalent catalysis, Acid-base catalysis, Strain / distortion in enzyme catalysis. Coenzyme catalysis.
8.	**Enzyme Inhibition:** Drug action through enzyme inhibition. Examples based on PDE4, GSK3, etc. Theories of enzyme inhibition and inactivation. Enzyme activation of drugs prodrugs.
9.	**Nucleic acids:** Nucleic acid as targets for drug action. Nucleic acid-interactive agents. Classes of drugs that interact with nucleic acids. Intercalation, Nucleic acid-alkylation, Nucleic acid-strand breaking and their importance in drug action.
10.	**Drug likeness:** Drug-like molecules and theories associated with the recognition of drug-like properties. Lipinski's rule, Veber rule, Ghose rule, CMC-like rule.
11.	**Drug action after Metabolism:** Physical organic chemistry of Drug metabolism, drug deactivation and elimination. Phase I and Phase II transformations. Concept of hard and soft drugs. Chemistry of ADME and Toxicity properties of drugs.
Recommended Books:	

1. The Organic Chemistry of Drug Design and Drug Action by R.B. Silverman
2. C. J. Coulson, Molecular Mechanism of Drug Action by C. J. Coulson
3. A primer of Drug Action by R.M. Julien
4. Drug-Receptor Thermodynamics by R.B. Raffa
5. Principles of Drug Action by W.B. Pratt, P. Taylor
6. Medicinal Chemistry How Drugs Act and Why by A. Gringauz
7. Principles of Molecular recognition by A.D. Buckingham
8. Quantitative molecular pharmacology and Informatics by M. Lutz
9. Physical Biochemistry by K.E.V. Holde
10. Free energy calculations in rational drug design by M. Rami Reddy

MC 511 - Spectral Analysis (2 Credits)

1.	**Ultraviolet (UV) and visible spectroscopy**:	
	(a)	Energy levels and selection rules: Definitions, molecular orbital approach for energy absorption, various modes of transitions.
	(b)	Correlation of structural variation with UV absorption: Factors influencing the position and intensity of absorptions, Inductive and resonance effects, effect of ring size, influence of stereochemical factors.
	(c)	Predicting UV absorption: Woodward-Fieser, Fieser-Kuhn and Nelson rules;
	(d)	Other factors: Non-conjugative effect, solvent effect, S-Cis band.
2.	**Infrared (IR) spectroscopy:**	
	(a)	Characteristic regions of the spectrum: Various modes of vibrations, Energy levels
	(b)	Correlation of structure with IR spectra: Influence of substituents, ring size, hydrogen bonding, vibrational coupling and field effect on frequency
	(c)	Applications: Determination of stereochemistry. Spectral interpretation with examples.
3.	**Nuclear Magnetic Resonance (NMR)spectroscopy:**	
	(a)	Fundamentals: Physical basis, magnetic nuclei, resonance, relaxation processes, signal-sensitivity.
	(b)	Instrumentation: Continuous-Wave (CW) instrument, Pulsed Fourier Transform (FT) instrument, Functions, Relation with sensitivity, Sampling.
	(c)	^{1}H NMR, correlation of structure with spectra: Chemical environment and shielding, chemical shift and origin of its concept, reference compound, local diamagnetic shielding and magnetic anisotropy, relation with chemical shift, chemical and magnetic non-equivalence, spin-spin splitting and its origin, Pascal's triangle, coupling constant, mechanism of coupling, integral, NMR solvents and their residual peaks, protons on heteroatoms, quadrupole broadening and decoupling, effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear coupling to ^{19}F and ^{31}P, virtual coupling, long range coupling-epi, peri, bay effects. Shift reagents-mechanism of action, spin decoupling and double resonance. Explanation of the spectra of some compounds, biomolecules and drugs.
	(d)	^{13}C NMR, correlation of structure with spectra: Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled ^{13}C spectra, Proton-decoupled ^{13}C spectra, Nuclear Overhauser Enhancement (NOE), Problem with integration, Distortionless Enhancement by Polarization Transfer (DEFT), Heteronuclear coupling for carbon to

		deuterium, carbon to ^{19}F, carbon to ^{31}P. Explanation of spectra of some compounds, biomolecules and drugs.
4.	**Mass spectrometry (MS):** Molecular ion and metastable peak, fragmentation patterns, nitrogen and ring rules, McLafferty rearrangement, electron and chemical ionization modes, applications	

Recommended Books:

1. Spectroscopy by Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan
2. Organic spectroscopy by William Kemp
3. Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
4. Spectrometric Identification of Organic Compounds by Robert M. Silverstein, Francis X. Webster& David J. Kiemie
5. Applications of Absorption Spectroscopy of Organic Compounds by Dyer
6. Fundamentals of Molecular Spectroscopy by Colin N. Banwell & Elaine M. McCash
7. Instrumental Methods of Analysis, Seventh Edition Hobart H. Willard, Lynne L. Merrit, John A. Dean and Frank A. Settle CBS Publishers
8. Edmond de Hoffmann, Vincent Stroobant: Mass Spectrometry, Principles and applications, 3rd Edition, Wiley, 2007.
9. Principles-of-Instrumental-Analysis-7th-edition-Skoog

MC 520 - Logic in Organic Synthesis-I (3 Credits)

1.	**Organic reaction mechanism**	
	(a)	**Hybridization**, Electron delocalization (Resonance)
	(b)	**Nucleophilic substitution reactions:** Uni- and bimolecular reactions; Attacking and leaving groups; Steric and electronic effects; Neighboring group participation; Formation and hydrolysis of esters, amides and acyl halides different mechanisms, Mitsunobu Reaction
	(c)	**Electrophilic substitution reactions:** Aromatic electrophilic substitutions including Friedel-Crafts reactions. Aromatic substitutions through Benzyne-radical substitution of arenes.
	(d)	**Addition and elimination reactions:** Addition to C=C and C=O; Mechanism; Dehydrohalogenation, dehydration, etc; E1, E2 and Syn-elimination mechanism, E1cB elimination. Regioselectivity in β-elimination reactions (orientation of π-bonds), Saytzeff and Hoffmann rules, elimination vs substitution, E1, E2, and E1CB comparative study, 1,1 elimination (α-elimination).
	(e)	**Methods of determining reaction mechanisms:** Kinetic and non-kinetic methods; Energy profile diagrams, Reaction intermediates, Crossover experiments and isotopic labelling; Order of reactions; Reversible, consecutive and parallel reactions; Solvent, ionic strength and salt effects; Acid-base catalysis
2.	**Principles of synthetic planning:** Logic-centered molecular synthesis; Dislocation, synthetic tree, synthons, logical imposition of boundary conditions, direct associated approach; Structure-functionality relationships, functionality and unsaturation levels; Polar reactivity analysis; Control elements, consonant and dissonant circuits; Protocol for synthetic design.	
3.	**Alkylation:**	
	(a)	**Enolates:** Regio- and stereo-selective enolate generation, "O" versus "C"- alkylation, effects of solvent, counter cation and electrophiles; Symbiotic effect; Thermodynamically and

		kinetically controlled enolate formations; Various transition-state models for stereoselective enolate formation
	(b)	**Enamines and metalloenamines:** Regioselectivity in generation, applications in controlling the selectivity of alkylation
4.	**Reaction of ylides:**	
	(a)	**Phosphorous ylides:** Structure and reactivity, stabilized and Non-stabilized ylides, effects of ligands on reactivity, Wittig reaction, Schlosser modification, Wittig-Horner and Horner-Wadsworth-Emmons olefination reactions, Mechanism of these reactions and E/Z selectivity; Petersons olefination, Application of Wittig-class of reactions and synthesis of various scaffolds.
	(b)	**Sulphur Ylides:** Stabilized and non-stabilized ylides; thermodynamically and kinetically controlled reactions with carbonyl compounds, regio- and stereo-selective reactions.
5.	**Hydroboration:** Control of chemo-, regio- and stereo-selectivity, rearrangement of alkylboranes; Alkylboranes as organometallic reagents, e.g., 9-BBN, thexylboranes, siamylborane, chiral boranes- Ipc_2BH $IpcBH_2$ etc.	

Recommended Books:

1. March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure by Michael B.Smith, and Jerry March
2. Designing Organic Syntheses by Stuart Warren
3. Organic Synthesis: The Disconnection Approach by Stuart Warren
4. Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism by Francis A. Carey; Richard J. Sundberg
5. Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism by Francis A. Carey; Richard J. Sundberg
6. Modern Synthetic Reactions by Herbert O. House
7. Modern Methods of Organic Synthesis by Carruthers, William Coldham, Iain
8. Mechanism and Structure in Organic Chemistry by Gould
9. Advanced Inorganic Chemistry by Cotton, Wilkinson, Murillo and Bochmann
10. Fundamentals of Medicinal Chemistry by Thomas ISBN047084307
11. ORGANIC. CHEMISTRY. Jonathan Clayden, Nick Greeves, and Stuart Warren.

In each case, the treatment of the topic starts from the entry-level discussion from the above text/ reference books followed by relevant research articles from the original research work as well as a review.

MC 530 - Separation Techniques (1 Credit)

1.	**Separation Techniques:** Need for learning separation techniques, separation techniques in natural product research and drug discovery, Extraction techniques.
2.	**Chromatography:** General principles and separation mechanisms, classification of chromatographic techniques, normal and reverse phase, bonded phase chromatography, stationary phases, stationary phases, Elutropic series
3.	**Column Chromatography:** Column packing, sample loading, column development, detection
4.	**Flash Chromatography and Vacuum Liquid Chromatography:** Objectives, optimization studies, selecting column and stationary phases, selecting suitable mobile phases, automated flash chromatography, and reverse-phase flash chromatography.
5.	**High Performance Liquid Chromatography:** Principles, instrumentation, peak shapes, capacity factor, selectivity, plate number, plate height, resolution, band broadening, pumps, injector,

	detectors, columns, gradient HPLC, HPLC solvents, sample preparation, method development, problems and troubleshooting.
6.	**Planar Chromatography - TLC/HPTLC/OPLC:** Basic principles, sample application, development of plates, visualization of plates, 2D TLC, densitometry, Over pressure layer chromatography.
7.	**Counter Current Chromatography:** Basic principles, droplet counter current chromatography, centrifugal partition chromatography, choice of solvents for SP and MP.
8.	**Gas Chromatography:** Principles, instrumentation, split-splitless injector, head space sampling, columns for GC, detectors, quantification
9.	**Biochromatography:** Size exclusion chromatography, ion exchange chromatography, ion pair chromatography, affinity chromatography general principles, stationary phases and mobile phases
10.	**Hyphenated Techniques:** Introduction to GC-MS and LC-MS techniques and their applications in natural products.

Recommended Books:

1. Methods in Biotechnology, Natural Product Isolation by Sarker, Latif, Gray
2. Methods in Biotechnology, Natural Product Isolation by Richard Canell
3. Various Reviews and Research Papers.

PE 510 - Pharmaceutical Preformulation - I (1 Credit)

1.	**Preformulation studies:** Preformulation studies of drug substances, proteins and peptides. Fundamental and derived properties in preformulation profiling. Preformulation work-sheet.
2.	**Role of pre-formulation in drug discovery:** material properties in lead selection, 'drugability' of new chemical entities, *in silico* and high-throughput pre-formulation studies
3.	**Role of preformulation in drug development:** Preformulation as a support for formulation development, identification of ‘developmental challenges’ during pharmaceutical development, dosage form-specific studies.
4.	**Salt selection:** Role of salt selection in drug discovery and development, theoretical concepts for selection of counter ions for salt formation, 'pKa rule' for salt formation, decision tree for salt selection, appropriate case studies.
5.	**Solubilization:** Solubility and solubilization of non-electrolyte, drug solubilization in surfactant systems, use of co-solvents for development of liquid formulations, solid-state manipulations including use of metastable solid forms like amorphous state.

MC 540 - Industrial Process and Scale-up Techniques (1 Credit)

1.	**Status of pharmaceutical industry:** Status of bulk drugs, natural products and formulations in India vis-a-vis industrialized nations.
2.	**Scale-up Techniques:** Pilot Plant Scale-up techniques: General Considerations including the significance of personnel requirements, Space requirements, raw materials, pilot plant scale-up considerations for solids, liquid orals, semi-solids, and relevant documentation. SUPAC Guidelines, Introduction to platform technology. Scale-up techniques for process optimization, maximization of productivity, in-process control techniques.
3.	**Chemical technology of selected drugs:** Case studies with emphasis on rationale for selection of routes, raw materials, process control methods, pollution control procedures etc.

4.	**Chemical technology of selected drugs:** Data collection during pilot plant trails, preparations of flow diagrams, material balance sheets and technical data sheets.
5.	Process technologies for some selected natural products of commercial interest, e.g. 4-hydroxyisoleucine, penicillin.
6.	Scale-up techniques for industrial pharmacy, typical standard operating procedures for different dosage forms; In-process control procedures.
7.	**Pharmaceutical manufacturing equipment:** Equipment used to manufacture bulk drugs and formulations.

Recommended Books:

1. Process Chemistry in Pharmaceutical Industry by Kumar Gadamasetti, Vol I & II
2. Advanced Organic Chemistry by Jerry March
3. Pharmaceutical Process Chemistry for Synthesis: Rethinking the Routes to Scale-Up by Peter J. Harrington, Wiley
4. Practical Process Research and Development by Neal G. Anderson, Academic Press
5. Strategies for Organic Drug Synthesis and Design by Daniel Lednicer

GE 510 - Biostatistics (2 Credits)

1.	**Statistics:** Introduction, its role and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation
2.	**Probability:** Basic concepts; Common probability distributions and probability distributions related to normal distribution
3.	**Sampling:** Simple random and other sampling procedures. Distribution of sample mean and proportion.
4.	**Estimation and Hypothesis Testing:** Point and interval estimation including fiducial limits. Concepts of hypothesis testing and types of errors. Student-t and Chi-square tests. Sample size and power
5.	**Experimental design and analysis of variance:** Completely randomized, randomized blocks. Latin square and factorial designs. Post-hoc procedures
6.	**Correlation and regression:** Graphical presentation of two continuous variables; Pearson's product-moment correlation coefficient, its statistical significance. Multiple and partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation and hypothesis testing for population slope. Introduction to the multiple linear regression model. Probit and logit transformations
7.	**Non-parametric tests:** Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal wallis and Friedman two-way anova tests. Spearman rank correlation
8.	**Statistical techniques in pharmaceutics:** Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control

Recommended Books:

1. Fundamentals of Biostatistics by Bernard Rosner
2. Pharmaceutical Statistics: Practical and Clinical Applications by Bolton and Bon
3. Statistical Misconceptions by Huck

GE 511 - Seminar (1 Credit)

1. Introduction, information retrieval systems
2. Writing term papers and reports
3. Organization of scientific material, thesis, dissertation and references
4. Reading research papers
5. Skill in oral presentation

Each student has to present a seminar before end of the semester.

LG 510 - General Laboratory Experience -15 hours/week (3 Credits)

1. **Analytical techniques: (75 hours)**
   (a) Spectral analysis workshop (45 hours).
   (b) Separation Techniques (30 hours)

2. (a) To provide training on various softwares used in specialization.

(*This portion will be covered by all the respective departments of the institute.*)

(b) Specialization (95 hours): Two to three-step synthesis involving Wittig reaction and glycidic ester condensation etc. Purification by chromatographic technique and identification by IR, NMR, and MS.

M.S. (Pharm.) Medicinal Chemistry
SEMESTER - II

MC 610 - Drug Design (2 Credits)	
1.	**Electronic Structure methods:** Quantum chemical methods semi-empirical and ab initio methods. Conformational analysis, energy minimization, comparison between the global minimum conformation and the bioactive conformation. Predicting the mechanism of organic reactions using electronic structure methods. Complete and constrained conformational search methods, their advantages and disadvantages. Theoretical aqueous solvation calculations for the design of ligands. Transition-state determination and their role in designing rigid analogs
2.	**Quantum chemical methods of analyzing drugs:** Metformin, its comparison to carbones, rapid racemization in glitazones, metabolism and toxicity of troglitazone, conversion of proguanil to cycloguanil
3.	**Molecular modeling:** Energy minimization, geometry optimization, conformational analysis, global conformational minima determination; approaches and problems. Bioactive vs. global minimum conformations. Automated methods of conformational search. Advantages and limitations of available software. Molecular graphics. Computer methodologies behind molecular modeling including artificial intelligence methods.
4.	**Structure Activity Relationships in drug design:** Qualitative versus quantitative approaches, advantages and disadvantages. Random screening, Non-random screening, drug metabolism studies, clinical observations, rational approaches to lead discovery. Homologation, chain branching, ring-chain transformations, bioisosterism. Insights into the molecular recognition phenomenon. Structure-based drug design, ligand-based drug design.
5.	**QSAR:** Electronic effects: Hammett equation, lipophilicity effects. Hansch equation, Steric effects. Taft equation. Experimental and theoretical approaches for the determination of physico-chemical parameters, parameter inter-dependence; case studies. Regression analysis, extrapolation versus interpolation, linearity versus non-linearity. Descriptor calculation. The importance of biological data in the correct form; 2D QSAR; 3D-QSAR examples of CoMFA and CoMSIA.
6.	**Molecular docking:** Rigid docking, flexible docking, manual docking. Advantages and disadvantages of flexible docking, Flex-X, Flex-S, Autodock and Dock softwares, with successful examples
7.	**Molecular dynamics:** Dynamics of drugs, biomolecules, drug-receptor complexes, Monte Carlo simulations and Molecular dynamics in performing conformational search and docking. Estimation of free energy from dynamical methods.
8.	**Pharmacophore concept:** Pharmacophore mapping, methods of conformational search used in pharmacophore mapping. Comparison between the popular pharmacophore methods like Catalyst/HipHop, DiscoTech, GASP with practical examples
9.	**De Novo drug design techniques:** Receptor/enzyme cavity size prediction. Predicting the functional components of cavities, designing drugs fitting into cavity
10.	**Informatics methods in drug design:** Brief introduction to bioinformatics, chemoinformatics. Their role in drug design.
Recommended Books: 1. Molecular Modelling, by A. R. Leach	

2. Organic Chemistry of Drug Design and Drug Action, by R.B. Silverman
3. Practical Applications of computer aided drug design, by P.S. Charifson
4. Molecular modeling in Drug Design, by C. Cohen
5. Chemical Applications of Molecular modeling, by J. Goodman
6. Pharmacophore perception, by O.F. Guner
7. An Introduction to Medicinal Chemistry, by Graham L. Patrick
8. Other suggested literature: Relevant research / review articles

MC 620 - Logic in Organic Synthesis-II (3 Credits)

1.	**Metal/ammonia reduction:** Reduction of mono-, bi- and tri-cyclic aromatic systems and various functional groups, reductive alkylation, regio- and stereoselectivity; Reduction of alkynes; Complex metal hydrides and selectrides.
2.	**Reaction of electron-deficient intermediates:** Carbene, nitrene and free-radical, their stabilities and modes of generation; Addition and insertion reactions of carbenoids and nitrenoids: regio- and stereo-selectivity, role of the metal catalysts in the transition-metal catalyzed reactions, other types of reaction of carbenoids, e.g., ylide generation, 1,3-Dipolar addition, rearrangement, etc.; Intra-molecular radical trapping process leading to ring annulation - Baldwin's rule.
3.	**Organometallics:** Applications of organo-lithium, cadmium and cerium reagents, heteroatom directed lithiation; Oxy- and amido-mercurations; Gilman reagent, mixed and higher order cuprates, uses in nucleophilic substitution, cleavage of epoxides and conjugate addition reactions; Spiro-annulation; Wacker oxidation, Wilkinson's catalyst, carbonylation/hydroformylation reactions; Catalytic and stoichiometric oxidation reactions; Homogeneous and heterogenous processes; Chemo-selective reactions; Bio-mimicing processes
4.	**Umpolung and umpoled synthons:** Concept, acyl and glycine cation/anion, homoenolate anion, vicinyl dicarbonian, carbonyl dication equivalence, etc. Umpolung of reactivity in carbonyl chemistry: Addition of electrophiles to carbonyl carbons, Enolate cations (use of ketene thioacetates, etc.), homoenolate anions (metalated allyl ethers amines, thioethers, silanes), bis-homoenolate cations.
5.	**Asymmetric synthesis:** Chiral induction factors controlling facial selectivity; Chiral reagents/catalysts, auxiliaries, enzymes and antibodies; Kinetic resolution, double asymmetric induction, acyclic diastereoselection, asymmetric amplification; Asymmetric synthesis of amino acids and *beta*-lactams
6.	**Pericyclic reactions:** Molecular orbital symmetry, frontier orbitals of 1,3-butadiene, 1,3,5-hexatrienes, allyl system, classification of pericyclic reactions; FMO approach, Woodward-Hoffman correlation diagram method and PMO approach to pericyclic reactions; Electrocyclic reactions-conrotatory and disrotatory motions, [4n], [4n+2] and allyl systems, secondary orbital interaction; Cycloaddition- antarafacial and the Suprafacial additions, [4n] and [4n+2] systems with stereochemical effects, 1,3 -dipolar cycloadditions, Cheletropic reactions; Sigmatropic rearrangements-supra and antarafacial shifts of H, Sigmatropic shifts of carbon moiety, retention and inversion of configuration, [3,3] and [3,5]Sigmatropic rearrangements, fluxional tautomerism, Ene reactions.
7	**Photochemistry:** Franck-Condon principle, Jablonski diagram, singlet and triplet states, photosensitization, quantum efficiency; Photochemistry of carbonyl compounds, Di-π-methane rearrangement, Norrish type-I and type-II cleavages, Paterno-Buchi reaction, photoreduction, photochemistry of enones and *para*-benzoquinones, Barton Reaction, Hofmann-Loffler-Freytag Reaction
7.	**Transition-metal-catalyzed C–C bond forming coupling reactions:** Organo-metallics (Pd, Ni, B, Sn, Zn, Si, Mg, etc) Name reactions: Suzuki, Negishi, Stille, Hiyama, Kumada, Heck, Sonogashira, Mechanism, Chemistry features, Conceptual variant reactions.

Recommended Books:

1. March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure by Michael B. Smith,

and Jerry March
2. Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism by Francis A. Carey; Richard J. Sundberg
3. Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism by Francis A. Carey; Richard J. Sundberg
4. Modern Synthetic Reactions by Herbert O. House
5. Modern Methods for Organic Synthesis, W. Carruthers and Iain Coldham
6. Asymmetric Synthesis, Vol 3, Editor: J. D. Morrison Advanced Organic Chemistry by March
7. Mechanism and Structure in Organic Chemistry by Gould
8. Advanced Inorganic Chemistry by Cotton, Wilkinson, Murillo and Bochmann
9. Fundamentals of Medicinal Chemistry by Thomas
10. ORGANIC. CHEMISTRY. Jonathan *Clayden* Nick Greeves Stuart Warren.

In each case, the treatment of the topic starts from the entry-level discussion from the above text/reference books, followed by relevant research articles from the original research work, as well as review articles published in peer-reviewed journals of international repute. Such suggested readings are provided along with the progress of the lectures

MC 630 - Structure and Function of Biomolecules (2 Credits)

1.	**Properties of amino acids and peptide bond**: End group determination of peptides, sequencing of peptides using various chemical and analytical techniques; Selected case studies like LHRH and TRH peptides
2.	**Protein structure building block to quaternary structure of proteins:** Ramachandran plots; Peptidomimetics; Protein-ligand interactions; Multiple binding modes
3.	Structure of lipoproteins and glycoproteins in relation to their function.
4.	**Structure of lipids, polysaccharides and carbohydrates:** Relationship between their physicochemical properties and their biological function
5.	**Detailed structure of nucleic acids and protein-nucleic acid interactions:** Nucleic acid andsmall molecule interactions with emphasis on approved drugs/drugs under advanced clinical stages; DNA damage and repair,
6.	**Structure and function of biomolecules pertaining to different therapeutic areas:** Cancer-tubulin inhibitors; farnesyl transferase- X-ray structure telomerase inhibitors, role of p53-MDM2 inhibitors, acetylcholine esterase, Aβ, and nucleic acid targeting drugs for neurodegenerative diseases disease ras protein and its role; Inflammation- COX-1 and COX-2 their structures and physiological role protein and topoisomerase-targeted antitubercular and antibacterial agents; Hyperlipidimia-HMG-CoA its structure and role in cholesterol manipulation
7.	**Methods for the determination of the structure of biomolecules:** **(a) Biological crystallography:** Crystallisation, data collection, refinement, identification of active site, phase determination heavy atom derivatives, electron density maps. Differences in the small molecule and biomolecule crystallography **(b) Spectrofluorimetry and Optical methods:** Basic principles of fluorescence, intensity, different fluorescent moieties, sensitivity of fluorescence to environment, biological applications in nucleic acid/protein labelling, staining and other molecular biology methods. High throughput screening of small molecules, binding constant and stoichiometry determination including Job's plot, Optical activity measurements, ORD/CD applications to Nucleic acids, proteins, and in studying drug-biomolecule interactions. UV-Visible spectroscopy and its applications in drug-biomolecule binding studies. **(c) Thermodynamic methods:** Differential Scanning Calorimetry (DSC) of biomolecules, Isothermal Titration Calorimetry (ITC). Various thermodynamics-based instrumental methods for drug-biomolecule energetics, specific and non-specific interactions, electrostatic and non-electrostatic

	contributions to binding, estimation of structural features of biomolecules, and enthalpy vs entropy contribution to free energy.

Recommended Books:

1. Physical Biochemistry: Applications to Biochemistry and Molecular Biology by David Freifelder
2. Methods in Modern biophysics, by B. Nolting
3. Introduction to Biophysical methods in Protein and Nucleic Acid research, by J.A. Glasel
4. Monosaccharides. Their Chemistry and Their Roles in Natural Products
5. Essentials of Glycobiology by Varki
6. Principles of Nucleic Acids by W. Sanger
7. Principles of Fluorescence Spectroscopy by J.R. Lakowicz

MC 650 - Stereochemistry and Drug Action (2 Credits)

1.	**Stereochemistry and Stereoisomerism**. Conformational isomerism and analysis in acyclic and simple cyclic systems - substituted ethanes, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane and decalins, optical isomerism - optical activity - molecular dissymmetry and chirality - elements of symmetry. **Fisher's projection D, L. and R, S. configurations** - relative and absolute configurations optical isomerism due to asymmetric carbon atoms - optical isomerism in biphenyls (atropoisomerism), allenes, and spirans - optical isomerism of nitrogenous compounds racemization and resolution - geometrical isomerism and E, Z configurations, properties of geometrical isomers, Chirality due to helicity **Molecular isomerism:** Molecular motion, time scales and energy, Conformation of open chain and saturated cyclic systems
2.	**Chirality and molecular symmetry:** Nomenclature and representations, Macromolecular stereochemistry, Dynamic stereochemistry
3.	**Group theoretical interpretation of chirality group:** Laws of group theory, symmetry elements and operations, classification of symmetry operation into groups, chiral and achiral point groups, determination of molecular structures into symmetry point groups platonic solids, desymmetrization
4.	**Conformational analysis:** (a) Definitions: Internal coordinates distinction between conformation and configuration (b) Conformational analysis of cyclic compounds: carbocycles and heterocycles, bi- and tricyclic compounds (c) Conformational analysis of acyclic compounds: potential energy diagrams of various acyclic systems, gauche effect, generalized anomeric effect
5.	**Assignment of configuration:** Various projectional formulae, molecular with chiral center, axis and plane.
6.	**Front on projectional formula of conformers and configurational isomers:** rational with specific examples.
7.	**Resolution procedures:** Biological and chemical; Analytical chiral integrity determinations; Pfeiffer rule and its violations; Recent attempts to develop continuous scale for chirality; Chiral ligands
8.	**Chirality and Drug Action:** Realization that stereoselectivity is a pre-requisite for evolution; Role of chirality in selective and specific therapeutic agents; Case studies; Enantioselectivity in drug absorption, metabolism, distribution and elimination.

Recommended Books:

1. Stereochemistry of Organic Compounds by Ernest L. Eliel, Samuek H. Wilen, Lewis N. Mander
2. Stereochemistry of Carbon Compounds by Ernest L. Eliel
3. Chemical Application of Group Theory by F. Albert Cotton
4. Relevant research articles as suggested time to time during the progress of classroom teaching.

PE 660 - Solid State Pharmaceutics (1 Credit)

1.	1. **Levels of solid-state properties:** Molecular / particle / bulk level properties, interdependence of various levels on each other, role of different levels during pharmaceutical development and process development 2. **Molecular level:** Crystalline form, definition, concept of long-range order, supramolecular arrangements, building blocks of crystals, unit cell, basic types of unit cells, demonstration of unit cells using crystal visualization softwares. 3. **Polymorphism**: Definition, significance of polymorphism in drug product performance, packing/ conformational polymorphism, thermodynamics of polymorphs, enantiotropy / monotropy, concept of transition temperature, Burger and Ramberger rule 4. **Crystallization process**: Molecular aggregation events in crystallization, energetic of crystallization, enthalpy entropy balance, types of nucleation, Ostwald's step rule, experimental protocols for polymorph screening 5. **Implications of polymorphism in pharmaceutical development**: Regulatory concerns related to polymorphism, introduction to latest regulatory position on polymorphism 6. **Amorphous state**: Definition, long range order versus short range order, disorder in the amorphous state, concept of glass transition temperature (Tg), thermodynamic necessity for Tg, entropy crisis. 7. **Role of amorphous state in drug delivery**: Solubility advantage, spring parachute effect during solubility studies, physical instability of the amorphous form, techniques for stabilization of amorphous form, amorphous solid dispersions. 8. **Co-crystals:** Introduction, synthons used for the formation of co-crystals and applications in drug delivery. 9. **Particulate level properties:** Crystal habit, generation of different crystal habits, implications of crystal habit on product performance and processing. 10. **Bulk level**: Bulk density, compressibility, flow properties, cohesivity, electrostatics, aggregation, agglomeration, role in formulation development and processing

Recommended Books:

1. Polymorphism in Pharmaceutical Solids Edited by Harry Brittain
2. Solid State Characterization of Pharmaceuticals Edited by Angeline and Mark Zarkrzewski
3. Crystal Engineering: A textbook, Edited by G. R. Desiraju, J. J. Vittal and A. Ramanan

PC 610 - Drug Metabolism (1 Credit)

1.	1. Biotransformation of drugs 2. Enzymes responsible for bio-transformations, microsomal and non-microsomal mechanisms. 3. Factors influencing enzyme induction and inhibition. 4. Factors effecting drug metabolism. 5. Drug metabolism in fetus and newborn. 6. Models to study drug metabolism. 7. Dose-effect relationships. 8. Excretion of drugs, biliary and fecal excretion. 9. Adverse drug reactions and drug interactions; Toxic reactions, allergic reactions, idiosyncrasy. 10. Acute poisoning and its treatment

Recommended Books:

1. Introduction to Drug Metabolism, by G. Gordon Gibson and Paul Skett
2. Drug Metabolism Handbook Concepts and Applications Edited by Ala F. Nassar, Wiley

GE 611 - Seminar (1 Credit)

Students are required to submit written record and present deta.ls of the project to be pursued in semester-Ill & IV This should include the purpose and basis of the project, stating aims, objectives and probable outcomes, be able to supplement these with necessary information, literature review towards it and process for the project itself.

LS 610 - General Laboratory Experience 10 hours/week (2 Credits)

Synthesis of a drug that includes 4 to 5 reaction steps; Isolation of each product by chromatographic and other techniques; Identification of the structure of products by spectral and other analytical techniques; Report of yield; Understanding the correlation between theoretical and practical aspects of chemistry. Study of theoretical organic chemistry using computation methods for the same reactions and learning the techniques of molecular modelling.